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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/444,934	05/22/95	LAWN	R MSM101CONTC

EXAMINER
JACOBSON, D

18M2/0816

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ART UNIT	PAPER NUMBER
1814	

DATE MAILED: 08/16/96

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on July 17,1996.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 4-6, 8, 20-30 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 4-6, 8, 20-30 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

Claims 4-6, 8, and 20-30 are pending in the present application.

The previous 35 U.S.C. 112, first paragraph, rejection regarding enablement has been withdrawn in light of applicants' arguments and upon further consideration by the examiner. The Rule 132 Declaration by Dr. Konigsberg has been considered.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as the specification, as originally filed, does not provide support for the invention as is now claimed.

Claim 4 is drawn to a tissue factor variant having "at least amino acid three to at least amino acid 219". The specification does not describe such a molecule, nor is there basis in the specification for this phrase. The specification discloses tissue factor variants lacking the transmembrane domain, i.e. residues 220-242 (page 13), insertional variants (page 12), specific point mutations (page 16), and glycosylation variants (page 16). The specification does not disclose other tissue factor variants.

Claim 20 is drawn to a molecule that has the sequence from amino acid one, two, or three to an amino acid between residues 219 and 263. The specification does not teach that functional tissue factor may begin at residues one, two, or three. This was not known at the time the invention was made. The specification also does not describe a molecule that ends at any point between residues 219 and 263.

Claim 27 is drawn to a protein consisting of residues three to 219. Claim 29 is drawn to a protein consisting of residues three to 263. Again, neither of these truncations are disclosed in the specification.

As discussed above, the specification discloses tissue factor variants that lack residues 220-242 (page 13), have specific insertions (page 12), have specific point mutations (page 16), or have altered glycosylation sites (page 16). The specification does not describe other tissue factor variants. Claims to other variants constitute new matter.

Claims 4-6, 8, and 20-29 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

In their amendment under 37 C.F.R. 1.192(a) applicants traverse the previous new matter rejection on the grounds that they have disclosed deletions of from one to thirty amino acids. Applicants argue that one of skill in the art would have been able to have deleted the cytoplasmic domain of the tissue factor protein. Applicants assert that "one would be hard pressed to argue why deletion of amino acids 220 to 263 would not be obvious from what is disclosed" (response of 5/22/95, page 8). Each of these arguments has been fully considered but is not deemed to be persuasive.

As discussed above, the specification describes deletion of the transmembrane domain, residues 220 to 242. Applicants have not *specifically* suggested other deletion variants. It is true that, following the methods described in the specification, one would be able to construct other deletion variants if one had the motivation to do so. Applicants have not provided any specific motivation to construct other deletion variants. In order to be enabling, a specification must stand on its own to suggest the claimed invention. Applicants have suggested that one to thirty

residues may be deleted, but without reference to particular residues. The mature tissue factor protein is 263 amino acids long and thus contains many possible fragments one to thirty amino acids long. One would need to construct all of the possible deletion mutants to identify those proteins that retain biological activity. Such would require undue experimentation.

The specification, as written, alone does not motivate one of skill in the art to construct deletion variants of tissue factor, in which, for example, residues 219 to 263 or 242-263 are deleted. At the time the invention was made, one would not have known these residues are not essential for biological activity of the protein. Although a restriction map may suggest cleavage of the nucleic acid molecule at a particular position, this does not indicate or suggest that the truncated protein will be biologically active.

Therefore, because applicants have not specifically disclosed other deletion variants of the tissue factor protein, claims to such are deemed to constitute new matter.

Claim 30 is rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to the disclosed tissue factor fusion proteins. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Claim 30 is drawn to tissue factor fusion protein. This includes any type of fusion protein, including tissue factor connected to a signal sequence or ligated to any other protein moiety. The specification suggests construction of a tissue factor fusion molecule consisting of a signal sequence, but does not suggest other types of fusion molecules. It is not known how the presence of other peptide sequences would affect biological activity of the tissue factor portion, i.e., if the presence of other peptide regions would interfere with tissue factor activity. Due to the lack of guidance set forth by the

specification regarding other fusion molecules, the many molecules possible, and the unpredictable nature of the art, it would require undue experimentation for one of skill in the art to construct, screen, and identify all of the fusion molecules encompassed by claim 30 that have activity in a clotting assay. Claim 30 is deemed to be beyond the scope of the enabling disclosure.

Claims 4-6, 8, and 20-30 are free of prior art. It is noted that claims to specific tissue factor variants lacking residues 220-242, or that have specific insertions, point mutations, or altered glycosylation sites may be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dian C. Jacobson whose telephone number is (703) 308-2973. The examiner can normally be reached Monday from 7:30 to 12:30 pm and Tuesday through Thursday from 7:30 to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at (703) 308-4216. The FAX number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Dian Jacobson

DIAN C. JACOBSON
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GROUP 1800